REMARKS

Attached hereto is a marked-up version of the changes made to the specification by the above amendment. The attached page is captioned **"Version with markings to show changes made."**

The amendment to claim 1 merely focuses the claims to the intended invention, which is directed to the concept of inhibiting viral infections by interference with viral integration into a target cell's genome. Claim 1 now incorporates this concept as found in original claims 2 and 6 and is supported at least page 51, Example 12 (pages 71 and 72), and Figure 19 of the application as filed.

New claims 8-21 are supported by the application as filed and are directed to preferred embodiments of the invention.

No new matter has been added and entry of the amendment is respectfully requested.

Notice to comply with sequence requirements

Applicants respectfully point out that a response to a Notice to comply mailed February 15, 2002 was filed March 13, 2002. Applicants are prepared to submit a postcard receipt in support of the previous response and/or re-submit the response as deemed necessary.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-7 have been rejected as allegedly indefinite as follows.

Claim 1 has been rejected as allegedly indefinite for use of the terms "viral DNA", "a virus", and "a viral vector" as well as the relative relationship of these terms. Applicants respectfully submit that when read in the light of the specification, and without reading limitations into the claims, the terms are clear to the skilled artisan as directed to the claimed methods of inhibiting the replication of the DNA of a virus by use of a conditionally replicating viral vector that interferes with the integration of the virus into the host cell genome. The terms "viral DNA" and "a virus" clearly relate only to the latter while "viral vector" clearly relates to the vector used to inhibit the virus.

Applicants respectfully note that the claims need not be limited to the use of a particular virus or a particular viral vector. Instead, all that is necessary is for the conditionally replicating viral vector to interfere with integration of the virus into a cell's genome.

The rejection with respect to claims 2 and 7 are moot in light of their cancellation.

The rejection with respect to claims 1-7 is respectfully traversed because most of the issues raised are not present in the language of the claims as they are currently pending. Of the language cited by the Examiner, Applicant notes that the invention is directed to the protection of cells by introduction of a conditionally replicating viral vector before the cell is infected by a virus. As such, there is no need to "determine whether a cell has a viral DNA". Additionally, there is no need to determine "viral vector DNA genomes integration" because the claims are directed to the use of conditionally replicating viral vectors that integrate as part of their replication cycle. The conditionally replicating viral vectors do not work based upon antigenicity or activation of the immune system, and as such, the Examiner's comments directed to those issues are not understood.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-7 have been rejected as allegedly limited to particular embodiments disclosed in the specification. Applicants respectfully traverse because the issues of the presence of ribozymes and the inhibition of all viruses and helper vectors in general is not material to the present invention, which is directed to the concept of inhibiting viruses by inhibiting their integration into a target cell's genome via use of a conditionally replicating viral vector that integrates into sites used by the virus. This is the concept of "direct interference" as described on page 51 and Example 12. The skilled person would understand that this is equivalent to a competition reaction where the lack of integration sites for a virus would prevent it from proceeding through its life cycle.

Of course the skilled artisan would also recognize that the claims are directed to the inhibition of viruses that have an integration step in their replication cycles.

The instant rejection has provided no objective reason why one skilled in the art would not be able to practice this invention in a manner commensurate with the scope of the claims. Accordingly, the emphasis on gene expression and alleged unpredictability thereof are not relevant to the instant claims.

Applicants therefore respectfully request withdrawal of the instant rejection.

Double Patenting Rejections

Claims 1-7 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-14 of U.S. Patent 5,888,767.

Claims 1-7 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-15 of U.S. Patent 5,886,806.

Claims 1-7 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-34 of U.S. Patent 6,114,141.

Claims 1-7 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-28 of U.S. Patent 6,168,953.

Claims 1-7 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-32 of U.S. Patent 6,232,120.

Applicants respectfully traverse because none of the cited patents teach, suggest or otherwise indicate the present invention directed to the inhibition of viral integration.

Accordingly, the instant claims cannot be patentably indistinct from the claims of the cited patents. Reconsideration and withdrawal of these rejections is respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 1-7 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Mautino et al. Applicants have carefully reviewed the statement of this rejection as well as the contents of the cited reference and traverse as follows.

Mautino et al. provide no teaching, suggestion or indication of a method to inhibit virus infection by interference with viral integration with a conditionally replicating viral vector. Mautino et al. discuss a number of possible mechanisms that contribute to their observed inhibition of HIV (see page 2035, paragraph bridging the two columns). None of those mechanisms, however, relate to the inhibition of viral integration. Accordingly, the cited reference fails to teach all of the limitations of the claims, and the instant rejection should be withdrawn.

Claims 1-7 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Dropulic et al. (USP 6,232,120).

As with the case of Mautino et al. above, Dropulic et al. provide no teaching, suggestion or indication of a method to inhibit virus infection by interference with viral integration with a conditionally replicating viral vector. Accordingly, the cited reference fails to teach all of the limitations of the claims, and the instant rejection should be withdrawn.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Dropulic et al. (WO 97/20060).

Once again, the cited reference by Dropulic et al. provides no teaching, suggestion or indication of a method to inhibit virus infection by interference with viral integration with a conditionally replicating viral vector. Accordingly, the cited reference fails to teach all of the limitations of the claims, and the instant rejection should be withdrawn.

Claims 1-3 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Welch et al.

Welch et al. disclose observations with respect to hepatitis C virus, an (+) strand RNA virus which does not integrate into a host cell genome as part of its replication cycle. The reference is thus directed to a different field of endeavor and unrelated to the instant claims. Accordingly, the cited reference fails to teach all of the limitations of the claims, and the instant rejection should be withdrawn.

Claims 1-3 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lieber et al.

Lieber et al. also disclose observations with respect to hepatitis C virus. Because there is no integration event possible in the viral replication cycle, the cited reference fails to teach all of the limitations of the claims, and the instant rejection should be withdrawn.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Venkatesh et al.

Venkatesh et al. also disclose the use of a conditionally cytotoxic adenovirus vector to kill cells upon infection with HIV-1. There is no indication that the integration of HIV-1 was inhibited by the adenovirus based vector. The cited reference fails to teach all of the limitations of the claims, and the instant rejection should be withdrawn.

Claims 1-3 and 6-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lu et al.

Lu et al. fail to disclose any effects relating to inhibition of HPV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Alwine et al.

Alwine et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Wong-Stahl et al.

Wong-Stahl et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Zhou et al.

Zhou et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Yu et al.

Yu et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Ramezani et al.

Ramezani et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lo et al.

Lo et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Dropulic et al. (PNAS 1996).

Dropulic et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Dropulic et al. (J. Virol.)

Dropulic et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Macpherson et al.

Macpherson et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Sczakiel et al.

Sczakiel et al. fail to disclose any effects relating to inhibition of HIV integration and thus fail to teach all of the limitations of the claims. Applicants request reconsideration and withdrawal of the instant rejection.

CONCLUSION

In light of the above amendments and remarks, Applicants believe that the claims are now in condition for allowance and urge passage of the application to issue. The Examiner is invited to contact Applicants' agent at the number listed below if it would be helpful in any way to resolve any remaining issue.

In the event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 397272000700. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 19, 2002

Respectfully submitted,

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Version with markings to show changes made.

Kindly amend the claims as follows:

1.(amended) A method of preventing or inhibiting the production of viral DNA in a cell infected with a virus by direct interference of said virus' integration comprising

introducing into said cell, before the cell is infected with said virus, a conditionally replicating viral vector that integrates into said cell as part of its replication cycle,

wherein said vector prevents or inhibits the production of viral DNA from copies of said virus that would have integrated into the cell's genome.